REMARKS

Claims 24-27, 49 and 57-61 and 63-68 are under examination and have been rejected. Claims 24, 26, 27 and 68 have been amended.

Claim Objection

The Examiner has objected to claims 67 and 68 as claiming duplicate subject matter. In response, Applicants have amended claim 68 to recite "macrophages" in place of "fibroblasts". Support for the claim to macrophages is found in claim 10 of the parent patent (U.S. 6,617,122) and in the specification at page 51, lines 9-14, and at page 54, lines 25-26.

Rejection Under 35 U.S.C. §112, ¶2

Claims 24-27, 49 and 57-66 were previously rejected under 35 U.S.C. §112, ¶2, as being indefinite for failure to recite an active method step to achieve the claimed treatment but, instead, only reciting how the treatment is to be effected. Applicants acknowledge the Examiner's withdrawal of this ground of rejection as to these claims.

Rejection Under 35 U.S.C. §101

Claims 24-27, 49 and 57-66 were previously rejected under 35 U.S.C. §101, as failing to recite a proper definition of a process. Applicants acknowledge the Examiner's withdrawal of this ground of rejection as to these claims.

Rejection Under 35 U.S.C. §112, ¶1

Claims 24-27, 49, 57-61 and 63-68 were rejected under 35 U.S.C. §112, ¶1, as failing to meet the written description requirement on grounds that they contain subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims were also rejected based on new matter and enablement.

In response, Applicant has amended claim 24 to more succinctly recite the claimed invention and clearly defined the agents whose use is intended. Applicants believe that those skilled in the art would recognize that Applicants were in possession of the claimed invention of amended claim 24 at the time of filing.

The Examiner suggests (see Office Action at page 5, last paragraph) that the claim does not specify if the agent is a small organic, an antisense molecule or an antibody. However, the claim recites that ABC1 activity is increased whereas the specification teaches that anti-sense molecules and antibodies decreased or abolished such activity (see Application at page 21, lines 10-25 (Figure 7 shows ABC1 activity greatly reduced by antisense molecules) and at page 51, lines 8-14 (reporting reduction of ABC1 biological activity in macrophages following antibody binding) so those skilled in the art would know enough not to use such molecules in practicing the invention.

The new matter rejection appears based mostly on use of the term "agent" and Applicants have amended this to recite "compound" in its place, for which the Examiner appears to concede enablement (Office Action at page 10, first paragraph).

The rejection as to enablement makes a number of points, mostly based on the requirements of *In re Wands* (Fed Cir 1988):

1. Breadth of the claims

Applicants have amended claim 24, and thus the other claims that depend from it, to specifically recite a compound binding to either ABC1 polypeptide itself or to a gene promoter for a gene encoding said polypeptide in a fibroblast or a macrophage (or monocyte) to increase phospholipid and/or cholesterol transport by said cell. The claims are drawn to a method of treating cardiovascular disease, or risk thereof, associated with low HDL-C by modulating ABC1, associated with low HDL-C by increasing ABC1-mediated cholesterol transport.

2. State of the Art and Level of Skill and Predictability

Applicants urge that the advantage of the teaching of the application is in knowing the specific activity of ABC1 that is to be modulated. The relevant art is highly skilled and, knowing that ABC1 has a physiological role on HDL-C levels, based on the application's teaching of cholesterol efflux and compounds like cholesterol analogs (see application at page 75, line 12), it is readily expected that agonists of this particular activity are the agents to be studied. That information was not known at the time the application was filed. For example, if cholesterol efflux and HDL binding of cholesterol are part of the ABC1 cholesterol transport activity (see application at page 28, lines 2-5, and at page 45) then clearly analogs of cholesterol and HDL are likely starting points. Given the advances of combinatorial chemistry and the specific screening assays already patented in the parent case, numerous compounds are readily prepared and tested. It should be noted that the claims are not drawn to a specific compound but rather to a way of treating cardiovascular disease associated with low HDL-C by modulating the cholesterol transport activity of ABC1.

3. Direction Provided by the Inventor and Working Examples

Heretofore, in the art other than the present application, the biological activities being screened for by skilled workers were of no use in treating cardiovascular disease. For example, other than Applicant's teaching, there was no evidence that known ABC1 activities (like anion transport) were related to cardiovascular disease. Applicants' key teaching is the determination of the physiological role of ABC1 in lipid, especially HDL-C, transport coupled with the already-established relationship between HDL-C and cardiovascular disease. Modulating an activity like cholesterol transport across cell membranes is fairly specific. The present application provides cell-based screening assays for modulators, such as enhancers, of ABC1-mediated cholesterol transport and such assays have been used to find positive modulators of ABC1 activity (see Bamberger patent below).

4. Quantity of Experimentation Needed to Make or Use the Invention

Claim 24 has been amended to recite modulation of phospholipid and/or cholesterol transport activity of ABC1 and because Applicants have identified the specific activity to be modulated (i.e., lipid transport) as well as the disease to be treated or prevented (i.e., cardiovascular disease associated with low HDL-C), the reactants and products of the reaction to be modulated have been identified. Intracellular cholesterol is the "reactant" and extracellular HDL-cholesterol is the "product" of the biological reaction at hand.

In support of the above remarks, Applicants direct the Examiner's attention to the Bamberger patent (Ref. A1 in Applicants' Form 1449 submitted 6 March 2006 and listed on the initialed sheets attached to the Office Action). Bamberger (U.S. 6,555,323) was re-examined (Control No. 90/007,595 – the claims were finally withdrawn) largely on the basis of Applicant's own application and issued patent (U.S. 6,637,122 – see Office Action in Bamberger re-examination dated 26 May 2006 starting at page 5 thereof).

In Bamberger, Table 1 identifies compounds that increase ABC1 activity (identified using essentially the same assay as Applicants herein although Applicants herein are entitled to an earlier priority date than Bamberger). Thus, the assays presented by Applicants herein clearly facilitate ready identification of positive modulators of ABC1 activity. For example, Bamberger reports (table 1 of the '323 patent) that cAMP and prostaglandin analogs increased ABC1 expression. Also, Applicants have pointed to use of cholesterol analogs as a starting point (see application at page 75, line 12).

Applicant respectfully request that the Examiner reconsider allowability of the pending claims in light of the claim amendments and above remarks.

Double-Patenting Rejection

The Examiner has requested that Applicants note other co-pending applications in this line of cases. Applicants believe that this information was included in the previous amendment. However, Applicant reiterates the requested information herein. Please note that one of the previously described co-pending applications is now abandoned.

Applicants respond that there are now 3 co-pending applications, each of which is a continuation of the original parent application that matured into U.S. Patent 6,617,122. The 3 co-pending applications are Serial No. 10/744,465 (filed 23 December 2003), 10/833,679 (filed 28 April 2004), and 10/452,510 (filed 2 June 2003). The status of these is:

1. Serial No. 10/833,679 (filed 28 April 2004) is recited in the Office Action (page 17, line 7 from bottom); a Terminal Disclaimer was filed.

2. Serial No. 10/744,465 (filed 23 December 2003) contains claims 1-35 drawn to a method of screening for ABC1 modulators using gene modulation and claims 36-45

(withdrawn) directed to treating diseases or disorders by administering an agent that modulates ABC1 activity wherein the agent was identified using one of the gene modulation assays claimed therein.

3. Serial No. 10/452,510 (filed 2 June 2003) contains claims drawn to substantially pure ABC1 polypeptides, polynucleotides, vectors and recombinant cells.

The Commissioner is authorized to charge payment of any fees required for this communication or credit any overpayment to Deposit Account No. 03-0678.

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